



MEMORANDUM

DATE: February 5, 2013

TO: The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)

FROM: Director, National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP)

SUBJECT: NIEHS Response to ICCVAM Test Recommendations for Identifying Chemical Eye Hazards with Fewer Animals

On September 19, 2012, at the request of the Secretary of the Department of Health and Human Services, I forwarded toxicological test recommendations from ICCVAM to 14 Federal agencies for their consideration. The recommendations were developed and transmitted pursuant to Section 3(e)(4) of the ICCVAM Authorization Act of 2000 (42 U.S.C. 285I-3). Pursuant to Sections 4(a) and 4(d) of the ICCVAM Authorization Act, agencies are required to review ICCVAM test recommendations and notify ICCVAM in writing of their findings, including identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted. This memorandum provides the NIEHS response to ICCVAM regarding the test recommendations.

ICCVAM provided recommendations for identifying chemical eye hazards with fewer animals, while maintaining eye hazard classification equivalent to that provided in current testing procedures specified in 16 CFR 1500.42 (CPSC 2010). ICCVAM recommendations are provided in the *ICCVAM Test Method Evaluation Report: Identifying Chemical Eye Hazards with Fewer Animals* (NIH Publication No. 12-7930). ICCVAM has also recommended pain management procedures that include the routine use of topical anesthetics, systemic analgesics, and humane endpoints that should always be used when it is determined necessary to conduct the rabbit eye test in the *ICCVAM Test Method Evaluation Report: Recommendations for Routine Use of Topical Anesthetics, Systemic Analgesics, and Humane Endpoints to Avoid or Minimize Pain and Distress in Ocular Safety Testing* (NIH Publication No. 10-7514). These procedures are expected to effectively eliminate pain and distress where *in vivo* ocular safety testing is required.

NIEHS agrees with ICCVAM that alternative *in vitro* test methods should always be considered and used where appropriate for eye safety testing. While currently approved *in vitro* test methods can identify some eye hazards (OECD 2009a, OECD 2009b), they are not sufficiently validated and accepted to completely replace all animal testing. When eye safety testing for those regulatory authorities still requiring the use of animals is necessary, testing should be conducted using the minimum number of animals in the most humane manner possible consistent with testing objectives. NIEHS agrees with ICCVAM that using a classification criterion of one or more positive animals in a 3-animal test to identify chemicals

and products that are eye hazards will maintain hazard classification equivalent to that provided by current testing procedures (16 CFR 1500.42 [CPSC 2010]), while using up to 50% to 83% fewer animals. ICCVAM therefore recommends, and NIEHS agrees, that the use of this classification criterion together with eye safety testing procedures that use a maximum of 3 animals per test substance should be considered. Consistent with ICCVAM's duty to foster national and international harmonization (42 U.S.C. 285l-3)), this recommendation also harmonizes the number of animals used for eye safety testing across U.S. regulatory agencies and international test guidelines.

NIEHS is not a regulatory agency and therefore does not promulgate regulatory testing requirements or guidelines for which the ICCVAM recommendations may be applicable. However, NIEHS appreciates ICCVAM's comprehensive evaluation for identifying chemical eye hazards with fewer animals and remains highly committed to the development, validation, and regulatory acceptance of scientifically sound safety testing methods that will support improved protection of people, animals, and the environment while providing for improved animal welfare.

/s/

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cc:

Dr. John Bucher, Associate Director, NTP
Dr. Warren Casey, Acting Director, NICEATM
Dr. Joanna Matheson, Acting Chair, ICCVAM